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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/934,114	08/22/2001	Roland K. McGready	2344-103	7926

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ROTHWELL, FIGG, ERNST & MANBECK, P.C.
1425 K STREET, N.W.
SUITE 800
WASHINGTON, DC 20005

EXAMINER
FOLEY, SHANON A

ART UNIT	PAPER NUMBER
1648	7

DATE MAILED: 04/08/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/934,114	MCGREADY, ROLAND K.	
	Examiner	Art Unit	
	Shanon Foley	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 January 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. *07/415,534* .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of group I in Paper No. 6 is acknowledged. Applicant's traversal is found persuasive and the restriction is withdrawn from consideration. Claims 17-30 are under consideration.

Specification

The disclosure is objected to because of the following informalities: The amendment submitted 1/21/3 lists the wrong filing date for application 07/415,354. Applicant lists the application in the preliminary amendment as filed on 9/15/89. However, 07/415,354 was filed 4/18/90 according to Office records. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 17-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 17, step (iv) states that the antibody classes are utilized as an immunogen. However, it cannot be determined what method steps are intended by this utilization. The claim also recites an "incubation system". However, the components of this system are not readily apparent. This rejection also affects claims 18-30.

Claims 29 and 30 recite that the "antibody exhibits a level of immunological activity". There is no definition for what is considered immunological activity of the antibody subclass and

a "level" of this activity cannot be readily determined. In addition, the "highest level of immunological activity" for these antibodies has no comparative basis. The specification provides no definition for what is intended by a "highest level" or a teaching for how to determine this level of immunological activation.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 29 and 30 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The claims state that the subclasses of antibodies exhibit a "level of immunological activity" and that the subclass with the "highest level of immunological activity" is selected. Although the specification discusses the immunogenic responses elicited by anti-paratopic antibodies bridging pages 5-6, there is no disclosure teaching the level of immunogenic properties of antibody subclasses prepared from (iii) of claim 17. Nor is there any teaching for determining a "level" of immunogenicity or how one skilled in the art would determine which subclass has the "highest level" of immunogenicity. Applicant is required to point to support for these phrases in the disclosure or cancel the new matter.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 17-30 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by McGready (WO 88/07058).

Claims 17-24 and 28-30 are drawn to a method of making anti-paratopic antibodies by:

(i) selecting a prototypic set of antibodies that specifically bind to an infectious etiological agent of interest, such as HIV, from a first species,

(ii) subdividing the paratopic set into antibody classes IgG, IgA, IgM, IgD and IgE, and one or more subclasses,

(iii) screening the classes to select the class(es) that specifically bind to an antigen, such as p18, p24, gp41, p55, gp120 and gp160 of the etiological agent HIV, and subjecting them to enzymatic cleavage to separate F(ab) fragments, which are used as an immunogen in the next step,

(iv) using the selected subclasses as an immunogen in a different species or in an *in vitro* spleen cells derived from the same or a different species to produce anti-paratopic antibodies from step (iii) antibodies, and

(v) selecting, isolating and purifying the anti-paratopic antibodies.

The spleen cells from step (iv) are harvested and fused to myeloma cells to form a hybridoma that produces monoclonal or polyclonal anti-paratopic antibodies.

Claims 25-27 are drawn to purified non-human anti-paratopic antibodies specific to an antigen from etiological agent or HIV.

McGready clearly anticipates a method of making anti-paratopic antibodies by selecting a prototypic set of antibodies from a first species that specifically bind to an antigen or specific

epitope of an infectious etiological agent of interest, such as HIV. McGready then teaches subdividing the paratopic set into antibody classes IgG, IgA, IgM, IgD and IgE, and one or more subclasses and screening the classes to select the class(es) that specifically bind to an antigen, such as p18, p24, gp41, p55, gp120 and gp160 of the etiological agent HIV. These immunoglobulins are subjected to enzymatic cleavage to separate F(c) fragments from F(ab) fragments, which are used as an immunogens in a different species or in an *in vitro* spleen cells derived from the same or a different species to produce anti-paratopic antibodies. McGready also clearly anticipates purified anti-paratopic antibodies derived from the method. The reference teaches fusing harvested spleen cells to myeloma cells to form a hybridoma that produces monoclonal or polyclonal anti-paratopic antibodies specific to an antigen from etiological agent or HIV. See claims 1, 6, 9-13, page 6, lines 17-23, page 7, lines 16-24, page 10, lines 15-8, Table 1 on page 11, page 12, lines 1-8, page 13, lines 7-21, page 16, lines 13 to page 18, line 9, Table 3 on page 20 and pages 26-29.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 17-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Essex et al. (US 4,743,678), Vander-Mallie (US 4,536,479) and Tunkanak et al. (Journal of Immunology. 1976; 117 (5), Part 1: 1664-1667).

See the summary of the claims above.

Vander-Mallie teaches a method of making an anti-idiotopic monoclonal or polyclonal antibodies by injecting antigens into animals to induce an antibody response in an animal (conventional immunization) or by fusing spleen cells with a myeloma cell line. Vander-Mallie also teaches that the antibodies produced "can be utilized as an immunoglobulin (Ig) fraction, an IgG fraction or as affinity-purified monospecific material." Vander-Mallie also teaches purified monoclonal and polyclonal antibodies produced by the method. See column 1, lines 20-27, column 3, line 54 to column 5, line 35 and column 7, line 1 to column 8, line 26. Vander-Mallie does not teach using F(ab) fragments of the antibody subclasses as immunogens in a different species or in the *in vitro* spleen cells.

However, Tungkanak et al. teach that anti-idiotopic responses in mice to a protein or a Fab-protein are indistinguishably in their specificity and sensitivity. Tungkanak et al. also teach that the Fc portion of the protein is not required for inducing anti-idiotopic antibodies. See the abstract and the discussion sections.

One of ordinary skill in the art at the time the invention was made would have been motivated to enzymatically separate the Fab fragments from the Fc potion fragments to induce a specific idiotypic antibody response that is equivalent to the antibody response induced by an antigen. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation for making anti-ioditopic antibodies in the method of Vander-Mallie with the Fab fragments of Tungkanak et al. because Vander-Mallie teaches the production of anti-idiotopic antibodies in two different hosts and Tungkanak et al. teaches that Fab fragments possess the same level of reactivity in two different strains of mice.

Neither Vander-Mallie nor Tungkanak et al. teach a specific antigen from HIV to develop the anti-idiotopic antibodies.

However, Essex et al. teach anti-idiotopic antibodies that are specific to HTLV-III (HIV) glycoproteins for use in diagnostic assays, see column 2, lines 4-6 and 13-28 and column 3, line 56 to column 4, line 4 and lines 21-34.

One of ordinary sill in the art at the time the invention was made would have been motivated to make anti-idiotopic antibodies specific to HIV glycoproteins taught by Essex et al. by the method disclosed by Vander-Mallie for use in diagnostic assays. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation for producing the instant invention because Vander-Mallie and Essex et al. teach that anti-idiotopic antibodies are monospecific for the antigen used, see column 1, line 65 to column 2, line 7 of Vander-Mallie and column 2, lines 4-6 of Essex et al.

One of ordinary skill in the art at the time the invention was made would have been further motivated to induce an immune response with a Fab fragment of Tungkanak et al. specific for the HIV glycoproteins taught by Essex et al. in the method of Vander-Mallie because Tungkanak et al. teach that Fab fragments induce the same antibody response generated by an antigen. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation for producing the instant invention because Tungkanak et al. teach that the Fab fragments are highly specific for the ligand-binding site of a protein and Vander-Mallie and Essex et al. teach that the ligand binding site of an anti-idiotopic antibody is responsible for its specificity, see column 1, line 46 to column 2, line 7 of Vander-Mallie and column 2, lines 18-28 of Essex et al. Therefore, the invention as a whole would have been prima facie obvious

to one of ordinary skill in the art at the time the invention was made, absent unexpected results to the contrary.

Applicant argues that neither Essex et al. nor Vander-Mallie teach separating prototypic antibodies that specifically bind to an etiological agent from all other antibodies present. Applicant argues that separating the antibodies into groups taught by Vander-Mallie or in the examples by Essex et al. do not meet the instant claim requirement.

Applicant's arguments as well as a review of the references have been fully considered, but are found unpersuasive. Essex et al. specifically teach anti-idiotopic antibodies are raised against first antibodies that are specific to the antigenic sites of the glycoprotein of the invention, see column 2, lines 23-26. The first antibodies of Essex et al. are identical to the instant prototypic antibodies specific for an etiological agent. The antibodies to the 45,000-52,000 and 61,000-68,000 dalton HTLV glycoproteins meet the instant claim limitation of the prototypic set having binding specificity for an etiological agent of interest, HTLV. Both Essex et al. and Vander-Mallie disclose monoclonal anti-idiotypic antibodies, see the previous citations. Monoclonal antibodies are highly specific and anti-idiotypic antibodies are highly specific to ligand binding sites of an antigen, see Vander-Mallie, Essex et al. and Tungkanak et al. Therefore, the monoclonal anti-idiotypic antibodies generated by Vander-Mallie and Essex et al. are not generated against any antibody present, but only those that bind a specific antigen of interest, such as the 45,000-52,000 and 61,000-68,000 dalton glycoproteins of HTLV. Therefore, it is determined that the monoclonal antibodies of Vander-Mallie and Essex et al. are pure products and the invention as a whole is prima facie obvious, absent unexpected results.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shanon Foley whose telephone number is (703) 308-3983. The examiner can normally be reached on M-F 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (703) 308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4426 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Shanon Foley
April 3, 2003

JAMES HOUSEL 4/7/03
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600